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# THE VIRULENCE OF DIPHTHERIA ORGANISMS IN THE THROATS OF WELL SCHOOL CHILDREN AND DIPHTHERIA CONVALESCENTS.\*

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IN spite of the lowering of the diphtheria death-rate due to the use of diphtheria antitoxin, and the immunity conferred upon those exposed to the disease when this substance is injected at a sufficiently early date, the fact still remains that the number of cases of diphtheria in all large cities is discouragingly high with a tendency to increase rather than to decrease. This increase in the number of reported cases is undoubtedly due very largely to the vigilance exercised by the more and more carefully organized boards of health, as indicated by the statistics of this city for the winters of 1902-5 inclusive. Here we find, in 1904-5, an increase in the number of cases reported with a marked decrease in the death rate. Expressed in tabular form the figures for the city as a whole are as follows:

TABLE 1.

Nov. 1 to March 1	Cases	Deaths	Mortality as per cent
1902-3 .....	798	127	16.0
1903-4 .....	1,254	204	16.3
1904-5 .....	1,517	103	12.7

It is impossible, at the present time, to assign an exact explanation for the decrease in deaths in 1904-5, but the most probable reason is the more extended and careful oversight of school children, who are now visited daily by medical inspectors, and a wider use of laboratory methods of investigation in cases of throat inflammations. Yet, with all the oversight that modern methods can give, outbreaks of the disease occur which cannot be well controlled, and sporadic cases crop up in all classes of society in which it is frequently impossible to locate the original source of infection.

It is generally agreed<sup>1</sup> that a small percentage of healthy persons

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<sup>1</sup> For thorough discussion of this subject see: J. A. Schabad, *Jahr. Kinderheil.*, 1901, 54, p. 381; G. S. Graham-Smith, *Jour. Hyg.*, 1903, 3, p. 217; *ibid.*, 1904, 4, p. 258; *Report of Mass. Association of Boards of Health*, on "Diphtheria in Well Persons," 1902; Alice Hamilton, *Jour. Infect. Dis.*, 1904, 1, p. 690.

harbor virulent diphtheria organisms; it is also undoubtedly true that a much larger percentage harbor organisms corresponding morphologically to the Klebs-Loeffler bacillus but which are not actively virulent for guinea-pigs. Whether these non-virulent or slightly virulent organisms are responsible for the transmission of diphtheria is a question upon which there is a voluminous and contradictory literature.

For the practical necessities of boards of health the question of the supervision of young school children as carriers of diphtheria is of the greatest importance. Thomas<sup>1</sup> states that 85 per cent of those children to whom infections might be traced were between five and eight years old, a period when the child is not subject to the sharp, rapidly developing form of the disease, as are younger children, but is apt to have a mild or even unrecognized attack during which it is not isolated and is, therefore, a fertile source of trouble.

Another difficult problem of the health officer is that of the release of the patient when he is recovered, or of the removal of the quarantine from his dwelling. Here the family, and often the physician, comes into conflict with those boards of health which require that the patient's throat shall be microscopically free from the diphtheria bacillus before the quarantine is removed. The physician states that the patient is quite well and longer isolation is therefore unnecessary. Sometimes he asserts that, though the dwelling is still quarantined, the patient is associating freely with members of the family and no evil results follow his harboring the disease germs.

For the purpose of collecting additional data upon these two questions—the virulence of diphtheria organisms in the throats of well school children, and the virulence of the organisms from a clinically well diphtheria convalescent—certain studies, which are outlined below, have been made in this laboratory.

#### THE VIRULENCE OF DIPHTHERIA BACILLI IN THE THROATS OF WELL SCHOOL CHILDREN.

During the months of January and February, 1905, cultures were taken by the majority of the 50 medical inspectors of the city of Philadelphia from the apparently normal throats of 375 public-school children. Of this number 40, or 9.3 per cent, showed, on microscopic examination, bacilli corresponding in morphology and staining peculiarities with Loeffler's bacillus.

<sup>1</sup> *Brit. Med. Jour.*, 1904, 2, p. 431.

Pure growths of these bacilli were obtained by sowing a small amount of the original culture in the water of condensation which formed in the bottom of a large tube containing a serum slant. This water, with its suspended organisms, was allowed to flow once over the surface of the serum and the tube was then placed upright in an incubator. From the comparatively few colonies appearing after 18 to 24 hours other sowings were made in a similar fashion until purity was obtained. Several colonies were transferred from tube to tube in order to insure the final presence of various varieties of the organisms if they existed in the original culture.

In 37 cases the organisms so obtained were inoculated into guinea-pigs. Most frequently the first culture received was worked up; occasionally, when the microscopic examination indicated the persistence of the germs, a second throat culture was independently inoculated to determine whether the virulence of the type had undergone any change. In every case tried the results of the second inoculation corresponded with those of the first. The inoculations were subcutaneous, using the growth scraped from a 24-hour old serum culture.

An endeavor was made to examine these throats until three consecutive negative results were obtained. In only eight cases was this successful, the others furnishing positive results constantly, or very rarely negative. For some of the children the period of observation extended over 40 days; the average time for all the cases was 23 days.

Out of 37 inoculations made in duplicate 13, or 35 per cent, failed to kill either pig, though some of them lost weight. Of the remaining 24 five killed both animals promptly. Nineteen killed one of the two pigs after a period varying from 3 to 14 days, the other pigs surviving though there was a marked loss in weight and frequently a pronounced edema at the site of inoculation. On these pigs, as well as on those in which the infection terminated fatally, the wound healed slowly, though at autopsy the organism was frequently found quite pure.

An examination of the animals which died promptly gave a fairly typical picture of a diphtheritic infection; when they survived for from 10 to 14 days, or, in a few instances, even longer, the edema at the site of inoculation had largely disappeared and a small amount of inflammation remained. This was often covered by a gray, necrotic deposit that extended over the originally edematous area. In this membranous deposit at the site of inoculation the original organisms could invariably be found. They were not found in the body fluids nor in any of the organs. The kidneys were usually hyperemic, occasionally the capsule was slightly adherent, the suprarenals were always much injected and often the heart was greatly enlarged with gorged arteries or a fatty degeneration.

Reference to the protocol which follows will show that 19 of the 50 medical inspectors had one or more positive cases, the maximum for an individual being six. Twenty-five schools were represented and nine of them had more than one pupil showing these organisms. Of the 40 cases examined one child had been in undoubted contact with a diphtheric child next door; seven cases had diphtheria in the immediate neighborhood of their dwellings; 10 had a history of diphtheria in the same school either at the time the first culture was taken or within a short period of it. One case developed clinical signs of diphtheria, but the organism failed to kill guinea-pigs though it was tried twice. Another case had had "tonsillitis" about the time of the first examination, but bacteria obtained from this throat proved non-pathogenic.

TABLE 2.

Serial Number	Age, Sex, Name	Microscopic Examination of Cultures with Dates	Animal Inoculation	Name of School	Cases of Diphtheria in This School	Cases of Diphtheria in the Family	Cases of Diphtheria in the Neighborhood	Schools or Employment of Family	Remarks
29,872	8 F. D. H.	1-5-05 + 1-7-05 -	Two pigs; lost weight, but recovered after 6th day Not inoculated	Nichols' Annex	None	None	None	Two infants at home	Deafness of patient
29,891	M. P. B.	1-5-05 + 1-8-05 +	One pig gained steadily for 17 days; the other lost wgt. slightly	Powers School	.....	None	None	Two brothers in Powers School	Had clinical evidence of mild case of diphtheria before first culture was taken
29,900	M. E. S.	1-5-05 + 1-7-05 + 1-31-05 +	Four pigs; 3 died. Average time 5 days. Other pigs sick, but pulled through	Muhlenberg School	None	None	Three cases in 3 houses opposite the school. One case fatal	Five children; all attend this school; 1 baby at home	No known contact between this child and cases cited; throat normal. Had <i>impetigo contagiosa</i> on chin
29,917	6 M. W. F.	1-6-05 + 1-10-05 -	Two pigs; sick for a few days, but recovered	Clay School	Two cases between September and January. One child excluded because of case in family	Sister had "sore throat" with membrane and positive culture	One case half a block from home	Sister in this school; 2 in Weccacoe school. 2 infants at home	Out of school "because of illness", for a couple of weeks. Complained of sore throat when he returned
29,936	6 F. G. K.	1-6-05 +	Two pigs; lost weight slightly	Wm. McClellan School	None	None	None	One brother and 4 sisters in this school; 2 sisters doing mill work .....	Headache and coated tongue
30,022	8 M. A. H.	1-6-05 + 2-4-05 -	Four pigs; not affected	Adams School	None	None	Brother in this school	.....	Associated with child in adjoining house who, 1-16-05, had "sore throat" with 2 positive cultures, but was not quarantined. 2-8-05 this child's throat was clear
30,017	7 F. M. T.	1-7-05 + 2-7-05 + 2-8-05 + 2-9-05 + 2-10-05 - 2-11-05 +	Four pigs; not affected	James Lynd School	None	None	None	.....	

TABLE 2.—Continued.

Serial Number	Age, Sex, Name	Microscopic Examination of Cultures with Dates	Animal Inoculation	Name of School	Cases of Diphtheria in This School	Cases of Diphtheria in the Family	Cases of Diphtheria in the Neighborhood	Schools or Employment of Family	Remarks
30,008	M. E. D.	1-7-05 + 2-9-05 - 2-10-05 +	Two pigs; neither much affected	Bartram School	One case, about the time the first culture was taken	None	About one mile away	Sister in Kindergarten School, and 2 brothers in Morton and Bartram respectively	
30,076	12 M. R. W.	1-10-05 + 1-11-05 + 1-31-05 + 2-7-05 -	Two pigs; died in 3 and 7 days respectively	Northwest School	None	None	None	One brother, 11th and Moore St. School; 1 sister, 7th and Dickinson St. School	
30,089	9 M. R. S.	1-10-05 + 1-31-05 - 2-10-05 - 2-11-05 -	Two pigs; 1 gained, other did not	Francis Reed School	None	None	None	Three children all in Ramsay School	
30,090	10 M. S. M.	1-10-05 + 2-1-05 -	Two pigs; 1 died, 1 recovered	Ramsay School	None since 12-23-04	None	None	Brother and sister in New Street	
30,088	4 F. E. G.	1-10-05 + 1-11-05 + 1-17-05 + 1-19-05 +	Two pigs; 1 died in 3 days, other survived	New Street School	One case	.....	.....	Primary School Northwest	
30,105	F. H. M.	1-10-05 + 1-11-05 - 2-9-05 +	Two pigs; 1 died on 8th day, others survived	Shippin School	None	None	None	Five children in Washington School; 1 sister in factory, 1 brother in poolroom	
30,109	F. M. DeG.	1-10-05 + 1-14-05 - 2-8-05 -	Two pigs; not affected	Washington School	None	None	None	Infant brother and sister at home	
30,149	6 M. T. B.	1-11-05 +	One died 13th day; other survived	Horace Binney School	None	None	None	Three brothers in New Street Primary	
30,204	M. H. S.	1-12-05 + 1-17-05 + 2-9-05 +	Two pigs; died on 7th and 8th days respectively	New Street Primary	One case	None	.....		

TABLE 2.—Continued.

Serial Number	Age, Sex, Name	Microscopic Examination of Cultures with Dates	Animal Inoculation	Name of School	Cases of Diphtheria in This School	Cases of Diphtheria in the Family	Cases of Diphtheria in the Neighborhood	Schools or Employment of Family	Remarks
30,195	11 M. G. S.	1-12-05+ 2-2-05+ 2-8-05— 1-12-05+	Two pigs; one died on 11th day, other sick	Ramsay School	Not since 12-23-04	None	None	One brother in Ramsay School	
30,206	5 F. S. Z.	1-12-05+ 2-2-05+ 2-8-05— 2-10-05+	Two pigs; one died in 9 days, other sick	New Street Primary	One case	.....	.....	Only child	
30,257	M. J. C.	1-12-05+ 1-19-05— 2-10-05+ 2-8-05— 1-13-05+ 2-2-05— 2-8-05— 2-9-05— 2-10-05—	Two pigs; not affected	Boon's Dam	Yes; about the time of first culture	None	Half a mile away	Three brothers in shops and a foundry	
30,257	M. D. R.	1-14-05+ 1-19-05— 1-14-05+ 2-8-05— 2-9-05— 2-10-05—	.....	Boon's Dam	Yes; about the time the first culture was taken	None	Half a mile away	Two children in Boon's Dam School; brother in soap factory, sister at home	
30,319	L. V.	1-14-05+ 1-19-05— 1-14-05+ 2-8-05— 2-9-05— 2-10-05—	Two pigs; not affected	Bartram School	Yes	None	None	Brother in factory	
30,324	6 M. F. M.	1-14-05+ 1-19-05— 1-14-05+ 2-8-05— 2-9-05— 2-10-05—	Two pigs; one died on 17th day	A. D. Bache	None	None	None	Brother and sister; one in Rache School	
30,328	7 F. T. J.	1-14-05+ 1-18-05+ 1-20-05+ 1-22-05— 2-7-05+ 2-8-05— 2-9-05+ 2-10-05— 2-11-05— 2-14-05— 1-17-05+ 1-31-05+ 2-9-05+ 2-11-05— 2-14-05+ 1-17-05+ 1-31-05+ 2-2-05+ 2-8-05+ 2-10-05—	Two pigs; died on 14th and 17th day, respectively	Baldwin School	Three cases on following dates: 12-21-04 12-28-04 1-16-04 Not, however, in this child's room	None	Three in immediate neighborhood	Only child	When first culture was made had fever and sick stomach; chronic catarrh and atrophied tonsils
30,393	7 M. W. McK.	1-14-05+ 1-18-05+ 1-20-05+ 1-22-05— 2-7-05+ 2-8-05— 2-9-05+ 2-10-05— 2-11-05— 2-14-05— 1-17-05+ 1-31-05+ 2-9-05+ 2-11-05— 2-14-05+ 1-17-05+ 1-31-05+ 2-2-05+ 2-8-05+ 2-10-05—	Two pigs; neither affected	Child's School	None	None	Four cases in immediate neighborhood	One brother in this school; baby at home	Had acute tonsillitis in January; on Feb. 8 he states that "now the baby is ill"
30,385	9 F. M. J.	1-14-05+ 1-18-05+ 1-20-05+ 1-22-05— 2-7-05+ 2-8-05— 2-9-05+ 2-10-05— 2-11-05— 2-14-05— 1-17-05+ 1-31-05+ 2-9-05+ 2-11-05— 2-14-05+ 1-17-05+ 1-31-05+ 2-2-05+ 2-8-05+ 2-10-05—	Two pigs; neither affected	Agnew School	None	None	None	One brother in this school	

TABLE 2.—Continued.

Serial Number	Age, Sex, Name	Microscopic Examination of Cultures with Dates	Animal Inoculation	Name of School	Cases of Diphtheria in This School	Cases of Diphtheria in the Family	Cases of Diphtheria in the Neighborhood	Schools or Employment of Family	Remarks
30,408	7 M. W. Y.	1-17-05 + 2-1-05 + 2-4-05 + 2-8-05 - 2-14-05 + 2-17-04 + 12-17-04 +	Two pigs; one died on 5th day, other nearly died	Ramsay School	None	None	None	One, sister in this school	
30,488	7 F. J. C.	1-18-05 + 2-1-05 - 2-8-05 - 2-10-05 - 2-11-05 - 2-12-05 -	Two pigs; neither affected	Jackson School	None	None	One case near dwelling	One, sister in this school	
30,489	8 F. R. M.	1-18-05 + 2-1-05 - 2-8-05 - 2-10-05 - 2-11-05 - 2-12-05 -	Two pigs; neither affected	Morton School	None	None	Two cases near dwelling	One sister in Morton School, another in Morton School	
30,498	5 F. A. O.	1-18-05 + 2-1-05 - 2-8-05 - 2-10-05 - 2-11-05 - 2-12-05 -	Two pigs; neither affected	Morton Primary	None	None	None	One sister in Morton School	
30,504	6 F. B. G.	1-18-05 + 2-1-05 - 2-8-05 - 2-10-05 - 2-11-05 - 2-12-05 -	Two pigs; neither affected	Adams School	None	None	None	Brother in this school	
30,505	6 M. F. McM.	1-18-05 + 2-1-05 - 2-8-05 - 2-10-05 - 2-11-05 - 2-12-05 -	Two pigs; not affected	Benson School	None	None	None		
30,509	6 F. E. K.	1-18-05 + 2-1-05 - 2-8-05 - 2-10-05 - 2-11-05 - 2-12-05 -	Two pigs; both died on 6th day	Geo. L. Horn School	None	None	None	Three brothers and 1 sister doing mill work, 3 sisters at home	On 1-10-05 a child was excluded from this school because his brother had membranous croup
30,515	M. E. E.	1-18-05 + 2-1-05 - 2-8-05 - 2-10-05 - 2-11-05 - 2-12-05 -	Two pigs; not affected	Nichols' Annex	None	None	None	One, sister in Nichols School	Had tonsillitis about time first culture was taken
30,540	7 M. H. M.	1-18-05 + 2-1-05 - 2-8-05 - 2-10-05 - 2-11-05 - 2-12-05 -	Two pigs; one died 14th day, other lost weight	Levering School	None	None	Brother and sister in department store and iron foundry, 2 children in this school		



TABLE 2.—Continued.

Serial Number	Age, Sex, Name	Microscopic Examination of Cultures with Dates	Animal Inoculation	Name of School	Cases of Diphtheria in This School	Cases of Diphtheria in the Family	Cases of Diphtheria in the Neighborhood	Schools or Employment of Family	Remarks
30,542	7 F. S. R.	1-19-05 +	Two pigs; 1 died on 12th day, other lost weight	Mühlenberg School	None	None	See 29,926	See 29,926	Brother of case 29,926
30,901	9 M. A. R.	2-9-05 + 2-11-05 -	Two pigs; not affected	.....	None	.....	.....	.....	Companion of cases 30,901 and 29,926
30,966	7 F. U. K.	2-11-05 +	Two pigs; one died on 11th day	Horace Binney School	None	.....	.....	One sister in this school	
30,150	6 M. H. B.	1-11-05 + 1-14-05 -	Two pigs; one died on 8th day, other lost weight for 5 days	Horace Binney School	None	None	None	Infant brother and sister at home	
30,159	7 M. H. R.	1-11-05 + 1-18-05 - 1-25-05 -	Not inoculated		None	None	None		

It has seemed desirable in the prosecution of this study to examine simultaneously a few schools located in widely separated neighborhoods and attended by different classes of children, to determine, if possible, the relation of the presence of the organism to environment. Four schools were selected, all admitting both boys and girls and having an individual attendance of from 750 to 1,300 children. Cultures were taken from normal throats and examined as before, except that the inoculations were made subcutaneously with 1 c.c. of a 24-hour broth culture as well as with the serum growth in a skin pocket.

One hundred and twenty-five children were examined; 13, or 10.4 per cent, showed, on microscopic examination, the presence of diphtheria organisms. Those harboring the bacilli were distributed among the four schools as follows;

Kane School . . . . .	2.5 per cent
William Cramp School . . . . .	9.7 "
Mantua School . . . . .	14.8 "
Geo. M. Wharton School . . . . .	18.5 "

There is indicated here a direct ratio between the social condition of the children and the prevalence of the organism in their throats. The Kane School, having about 800 boys and girls, is attended by cleanly, well-kept children, mostly of well-to-do parents; the Geo. M. Wharton School draws its 1,300 scholars very largely from among the Poles, Italians, and Russian Jews, who are crowded into most unsanitary surroundings. The other two schools show intermediate social conditions and the percentage of infected throats corresponds.

The general average for the four schools is 10.4 per cent of persons harboring the organisms; a figure agreeing closely with that found in examining children haphazard all over the city. A comparative table of results obtained in the two series illustrates this point more clearly.

	Four selected schools	Twenty-five schools at random
Organisms killing guinea-pigs . . . . .	15.3 per cent	13.5 per cent
Organisms showing some pathogenicity . . . . .	30.7 "	51.3 "
Organisms without virulence . . . . .	53.0 "	35.1 "
Children infected . . . . .	10.4 "	9.3 "

For the cultures from the throats of these children and the histories of those carrying diphtheria organisms I am indebted to the corps of medical inspectors, and especially to Drs. Coates, Cornell, Fretz, and O'Hara.

#### THE VIRULENCE OF DIPHTHERIA ORGANISMS IN THE THROATS OF CONVALESCENTS.

The organisms obtained from the throats of 25 individuals clinically recovered from diphtheria were tested for virulence. Whenever possible they were isolated from the culture just preceding the condition required for release from quarantine. In several instances the organisms were isolated at different times during convalescence and their virulence tested for a diminution in activity. In only one case was such a loss of virulence noted.

Nine of the 25 cases were sent to the laboratory by the medical inspectors for release from quarantine. For the histories of the other 16 as well as the cultures used in this work I am indebted to Dr. B. F. Royer, chief resident physician at the Municipal Hospital.

Twenty-two of the 25 cases examined gave virulent organisms. In 15 of the 22 they were tested on their last appearance and in the others only a few days elapsed after

TABLE 3.

No. of Scholars Examined	Age, Sex, Name	Microscopic Examination of Cultures with Dates	Animal Inoculations	Name of School	Cases of Diphtheria in This School	Cases of Diphtheria in the Family	Cases of Diphtheria in the Neighborhood	Schools or Employment of Family	Remarks
31	11 M. J. H. H. F.	2-23-05+ 3-3-05- 3-7-05- 3-8-05- 2-23-05+	No effect	Wm. Cramp	None	None	None	One brother in same school; other a laborer	This child attended a Sunday school in which was a case of diphtheria about this time
	12 M. A. B.	3-1-05+ 3-3-05- 3-7-05- 3-8-05-	2 pigs; lost weight, with induration at site of inoculation	Wm. Cramp	None	None	None	Sister in Taylor School; brother in this school	
	12 F. I. D.	3-8-05+ 3-10-05+	2 pigs; marked loss of weight	Kane	None	None	None	Sister in a mill	
	10 M. T. M.	2-27-05+ 3-14-05-	No effect	Geo. M. Wharton	None	None	None	Sister in same school	Had sore throat a short time before; 8 cases of 'sore throat' in this child's room in Kane school; 5 of these examinations showed streptococci but no Klebs-Löffler
27	9 M. P. Z.	2-27-05+	No effect	Geo. M. Wharton	None	None	None	Four brothers and 2 sisters; all working in various establishments and all over 14 years	Parent has very large tonsils.
	9 M. B. G.	2-27-05+ 3-14-05+	No effect	Geo. M. Wharton	None	None	.....	Four sisters; 2 in school. Mother recently had grippe	
	10 M. A. H.	2-27-06+ 3-14-05-	1 pig showed necrosis and loss of weight; other died in 3 days. Typical diphtheria	Geo. M. Wharton	None	None	.....	One sister; at house; no illness in family	Four families live in this child's house. Scarlet fever one year ago.
	9 M. C. H.	2-27-05+ 3-14-05-	2 pigs died in 2 days	Geo. M. Wharton	.....	.....	.....	Sister and brother in this school; 1 brother in high school	Three families in this house. No illness at time of first culture.
27	8 M. C. W.	2-27-05+ 3-3-05- 3-6-05- 3-8-05-	No effect	Mantua	None	None	None	Two brothers, two sisters, all between 5 and 12 years; attend different schools. Father keeps saloon and boarding-house	
	7 F. S. N.	2-28-05+ 3-3-05- 3-6-05- 3-8-05C.	No effect on guinea-pigs	Mantua	None	None	None		
	7 M. F. R.	3-8-05+ 3-8-05+	Pigs lost weight; wounds necrotic	Mantua	None	None	None		
	6 F. C. M.	3-8-05+ 3-8-05+	Lost weight; wound did not heal for one month	Mantua	None	None	None		

TABLE 4.

Name and Serial Number	Microscopic Examination of Cultures with Dates	Animal Inoculations	Duration of Disease before First Culture for Disinfection Was Taken	Administration of Antitoxin	Remarks
V. H. 31,470	3-28-05— 3-29-05 C 3-30-05— 3-31-05+ 4-2-05— 4-3-05—	Two pigs, from culture taken 3-31-05; both dead in 3 days	Nine days	Satisfactory	
A. D. 31,463	3-18-05+ 3-21-05— 3-21-05—	One pig; died on second day; culture of 3-18-05 used	Fourteen days; clinical evidence gone on fifth day of disease	Satisfactory	
A. D. Jr. 31,464	3-18-05+ 3-21-05— 3-21-05—	One pig; died in 24 hours	Fourteen days	Satisfactory	
G. C. 31,436	3-16-05+ 3-17-05+ 3-21-05— 3-22-05—	Two pigs; culture of 3-16-05 used; both died in 2 days	Fourteen days; clinical evidence had disappeared on fifth day	Satisfactory	
C. O'C. 31,574	3-28-05+ 3-29-05+ 3-30-05+ 4-1-05+ 4-2-05+ 4-3-05+ 4-5-05— 4-6-05—	Two pigs, inoculated from culture made on 3-28-05; died on second day. two other pigs inoculated from culture of 4-31-05 also died on second day. One pig, from culture of 4-2-05, died second day	Eight days; fifth or sixth day when clinical signs disappeared	Satisfactory	
S. S. 31,502	3-23-05 C* 3-24-05+ 3-25-05+ 3-26-05+ 3-29-05— 5-30-05 C	Two pigs; both died in 5 days; organism from culture on 3-24-05 Two pigs inoculated from culture taken 3-28-05 died in 2 days	Fourteen days	Satisfactory	
S. van L. 31,264	3-4-05— 3-5-05— 3-7-05—	Two pigs inoculated from culture of 3-7-05; both died in 2 days	Seventeen days; clinical signs disappeared on tenth day	Satisfactory	
B. M. 31,176	2-27-05+ 3-1-05+ 3-3-05+ 3-4-05+ 3-5-05— 3-6-05 C 3-7-05+ 3-8-05— 3-7-05+ 3-8-05+ 3-14-05 I 3-15-05+ 3-22-05— 3-23-05+ 3-24-05— 3-25-05—	Two pigs inoculated from culture of 3-7-05; both died in 2 days	Thirteen days; child had been well for a week	Not given	
W. M. 31,294	3-7-05+ 3-8-05— 3-7-05+ 3-8-05+ 3-14-05 I 3-15-05+ 3-22-05— 3-23-05+ 3-24-05— 3-25-05—	Two pigs; died in 24 hours. Inoculated from culture taken on 3-8-05	Seventeen days; well for seven days	Satisfactory	
C. R. 30,212	3-6-05+ 3-7-05—	Two pigs, not affected	One hundred days; exudate disappeared on fifth day	Satisfactory	Admitted for diphtheria. Contracted scarlet fever while waiting for negative cultures
G. J. 31,259	3-16-05+ 3-17-05— 3-18-05— 3-21-05— 3-22-05— 3-15-05— 3-16-05+ 3-17-05— 3-18-05— 3-22-05+ 3-31-05— 4-1-05—	Two pigs; died in 24 hours	Throat cleared up ninth day of disease		
R. W. 31,261	3-15-05— 3-16-05+ 3-17-05— 3-18-05—	Two pigs; died in 22 hours	Eleven days	Satisfactory	
R. R. 31,422	3-22-05+ 3-31-05— 4-1-05—	Two pigs; died in 24 hours	Eleven days	Administered	

\*B. subtilis had liquefied the serum, making examination for diphtheria bacilli impossible.

TABLE 4.—Continued.

Name and Serial Number	Microscopic Examination of Cultures with Dates	Animal Inoculations	Duration of Disease before First Culture for Disinfection Was Taken	Administration of Antitoxin	Remarks
A. L. 31,426	3-22-05+	Two pigs; died in 24 hours	Eight days	Administered	
	3-23-05—				
	3-24-05—				
J. McA. 31,540	4-3-05+	Two pigs; died in 48 hours	.....	Administered	
	4-4-05—				
G. McA 31,543	4-5-05—	Two pigs; inoculated from culture made 4-3-05. Both died on second day	Sixteen days; well for ten days	Administered	
	4-3-05+				
	4-4-05+				
	4-5-05+				
	4-6-05—				
	4-7-05+				
	4-8-05+				
	4-11-05+				
	4-13-05+				
	4-14-05—				
A. McA 31,544	4-15-05—	Two pigs; died in 24 hours; culture of 4-3-05 used	Fifteen days; no clinical signs for eight days	Administered	
	4-5-05+				
	4-4-05—				
	4-5-05+				
	4-6-05+				
	4-7-05+				
	4-11-05+				
	4-12-05—	Two pigs; not affected	One hundred and tenth day when cultured	Administered	A nurse in the diphtheria wards. Has continued to give an occasional positive culture for months after complete recovery from an attack of the disease
	4-13-05—				
J. C. 31,349	12-16-04+				
	12-21-04—				
	12-22-04+				
	12-23-04+				
	12-24-04+				
	12-26-04+				
	12-27-04+				
	12-28-04+				
	12-29-04+				
	1-4-05—				
	1-8-05+				
	1-9-05+				
	1-10-05+				
	1-12-05—				
	1-13-05—				
H. O.	4-3-05+	Two pigs; died in 48 hours	Seventeen days	Administered	
	3-17-05+				
	3-31-05—				
	4-3-05—	Two pigs; died in 48 hours	Six days	Administered	
	4-4-05—				
	4-5-05—				
K. R. 31,412	3-15-05—	Two pigs; inoculated from culture obtained 3-20-05. Died in 24 hours.	Twelve days; well for seven days	Administered	
	3-16-05—				
	3-17-05+				
E. R. 31,417	3-12-05+				
	3-13-05+				
	3-17-05+				
	3-20-05+	Two pigs; killed in 24 hours	Twelve days; no exudate for six days	Administered	
	4-3-05—				
	4-4-05—				
	4-7-05—				
F. S. 31,587	4-9-05—	Two pigs; died in 48 hours. Culture of 4-3-05 used	Fourteen days; no exudate for four days		
	4-10-05—				
	4-3-05+				
	5-4-05+				
	5-6-05+				
A. G. 31,585	5-7-05—	Two pigs; both died on second day	Thirteen days; no exudate for six days		
	5-8-05—				
	4-3-05+				
	4-14-05—				
R. T. 31,593	4-15-05—	One pig; died in 3 days; culture of 3-18-05. Two pigs inoculated with culture of 4-4-05 were not affected	Two consecutive negative cultures were never obtained; patient discharged when organism ceased to show virulence. Exudate disappeared on 5th day	Administered	
	2-28-05+				
	3-7-05—				
	3-8-05+				
J. A. 31,202	3-18-05+				
	4-4-05+*				

\*Continued positive until 5-19-05 when patient was discharged, eighty-fourth day.

the cultures had been taken before the throat was free of them. These final positive cultures were made from 5 to 17 days after the patients were recovered from the disease, the average time being nine days.

Two cases showed diphtheria organisms morphologically perfect, but they did not affect guinea-pigs. One of these patients was a nurse in the Municipal Hospital who contracted the disease and was released from quarantine on the 28th day, two consecutive negative cultures having been obtained. Frequently, however, cultures from her throat were found to be positive (see case J. C. 31,349), but the organisms when tested on the 110th day lacked virulence. The second case contracted scarlet fever while waiting for the organisms to disappear from his throat, all other signs of diphtheria having vanished. After complete recovery from scarlet fever the presence in the throat of organisms morphologically identical with Loeffler's kept him at the hospital for some weeks. One hundred days after all clinical signs of diphtheria were gone the organisms were isolated and inoculated into guinea-pigs. They were not active.

Case No. 31,202, J. A., gave 18 days after recovery a virulent organism. Microscopically the organisms persisted and were again tested 17 days later. This test showed absolutely no virulence. The case was kept under observation for 45 days longer, but the organisms had not, at the expiration of that time, disappeared.

#### SUMMARY.

Among well school children approximately 10 per cent harbor in their throats bacilli which correspond morphologically with the organisms of diphtheria.

One-half of these organisms are without effect on guinea-pigs. About 30 per cent behave like attenuated forms and 14 per cent kill the animals with a fair degree of promptness.

Of 25 strains of diphtheria bacilli obtained during the last days of convalescence 23 were highly virulent; 2 were without virulence, one being from the throat of a convalescent nurse constantly associating with diphtheria patients, the other from a case which had contracted scarlet fever while convalescing from diphtheria. One case gave a virulent organism on the 18th day and a non-virulent one on the 35th day.

In the report of the Massachusetts Association of Boards of Health on "Diphtheria Bacilli in Well Persons" is found the following paragraph: "As there is no sharp line to be drawn between the healthy and the diseased state, one shading imperceptibly into the other, so there is no sharp line to be drawn, for many infections at least, between the time when the micro-organisms are still in the body and when they have all been destroyed or eliminated. It follows logically, as is shown by the work of certain members of this committee, that

well persons may be at times the source of infectious diseases." In this very admirable paper the conclusion is also stated that the organisms in the throats of well persons recently exposed to diphtheria are likely to be virulent.

Such observations naturally lead to the consideration of the question of the increase or decrease in the virulence of the same strain of the diphtheria bacillus depending upon its environment. An absolute differentiation of the so-called pseudo-diphtheria bacillus from the diphtheria bacillus has not yet been accomplished. On the other hand, we meet with recent evidence that morphologically and clinically the most satisfactory pseudo-forms have a decided pathogenicity for guinea-pigs and, from clinical evidence, for human beings;<sup>1</sup> hence the harmlessness of these germs cannot be accepted unconditionally, any more than a certain virulence can be attached invariably to a diphtheria bacillus which agrees with some arbitrary requirements laid down by bacteriologists.

As long ago as 1890<sup>2</sup> Roux and Yersin showed that virulent diphtheria bacilli could be made quite harmless by an unfavorable environment and that a non-virulent organism, acting on a guinea-pig in conjunction with an organism of quite a different variety, such as the streptococcus of erysipelas, will become highly pathogenic.

More recently<sup>3</sup> Ohlmacher not only heightened the virulence of the bacillus by passage through a guinea-pig, but changed the morphology of a short, solid form to the slender curved variety; and conversely, inoculation of a granular form into a white rat changed the organisms to those having the short, pseudo-morphology.

Additional laboratory data to determine exactly the biological relation, if there be such, between the virulent and non-virulent diphtheria organisms is still greatly to be desired. Clinically it would seem to be fairly well established that well persons harboring diphtheria bacilli who have not been recently exposed to the disease, are occasionally responsible for a true diphtheric infection, but such cases are rare. It is also true that the organisms found in the throat of a well person not exposed are, in the majority of cases, without virulence.

<sup>1</sup> Alice Hamilton, *Jour. Infect. Dis.*, 1904, 1, p. 670.

<sup>2</sup> *Ann. de l'Inst. Pasteur*, 1890, 4, p. 384.

<sup>3</sup> *Jour. Med. Res.*, 1902, 7, p. 128.

Those well persons who have been exposed to diphtheria and who carry the organisms in their throats, while perfectly well themselves, do, very frequently, harbor an organism of marked virulence and are responsible for many more infections than are the well, unexposed persons. Lastly, the convalescent from true diphtheria will carry and disseminate virulent organisms so long as any remain in his throat, which period may far exceed the duration of the clinical evidences of the disease.

It is required of those having in charge the public health that the majority shall be protected from disease with the minimum amount of inconvenience to the minority who are responsible for the spread of any infection. What these protective measures shall be must depend not only upon the infection to be combated but, very often, upon the conditions prevailing at the moment. The isolation of a clinically well diphtheria convalescent, while waiting for the organisms to disappear from the throat, frequently causes inconvenience and even hardship, but from the accumulated evidence on the subject there seems but one course to pursue, namely, to forbid association with non-immunes so long as the laboratory findings are "positive."

What course should be taken in regard to the well persons not exposed to diphtheria who carry bacilli is not so clear. To quarantine such a number would be impractical; yet the bacteriologist must insist that, in the absence of definite evidence to the contrary, the organism which is harmless and attenuated in the throat of a well individual may, if planted on another throat under different conditions of susceptibility, so increase in virulence that its specific disease is produced.

The best argument for the infrequency of such an increase in virulence, if, indeed, it ever happens, is the fact that so many well persons carry the organisms without apparent menace to their associates. In the case of school children, if medical supervision is possible, it would seem desirable that they be watched carefully for any clinical manifestations of diphtheria and that they should be taught personal habits which will render infection of others less likely.